

# Comparative Female Reproductive Tract Development and Morphology

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**A brief description of the basic pattern of mammalian organogenesis of the female reproductive tract is presented based on events as they occur in human beings. The emphasis is not on the details of this development, but rather its organization and timing. Tables of comparative development provide a comparison of similar events between man, rat, mouse, and chick.**

The major purpose of this presentation is to highlight the development of the female genital tract, providing enough of the basic framework of this delicately interwoven system to aid your personal pursuit of its details. To do so without discussing the development of either the kidney or the male genital system is clearly impossible, but reference will be made to the latter two systems only when it is necessary to indicate their essential interactions with the developing female system. Finally, tables are provided to allow a comparison of the timing of these events as they occur during the development of chicks, rodents and man although the discussion will be based on events as they occur in man. Some general references (1-9), not intended to be exhaustive by any means, which should aid in study of comparative mammalian embryology, are appended.

There are several key points or concepts upon which rests an understanding of the development of the female reproductive tract. These are (1) location within the embryo of the tissue from which the urogenital system including the gonads will develop, (2) induction of the female genital tract by the renal system and of the vagina by Mueller's tubercle, (3) migration of the germ cells from the yolk sac to establish the gonad, and (4) differentiation of the cloaca into the external genitalia. These concepts will be emphasized as this presentation develops.

As was stated previously, no discussion of the development of the reproductive system, whether it be male or female, can ignore the developing kid-

neys, for these two components of the urogenital system are united both through their common origin within the intermediate mesodermal ridge and the inductive interactions mentioned above. The location of these intermediate mesodermal ridges or mesomeric ridges is ventral to the developing central nervous system, on each side of (bilateral to) the aorta. These two ridges bulge into the coelomic or developing abdominal cavity dorsal to the developing gut and stretch the length of the cavity to join with one another in the region of the urogenital sinus. Within this mesomeric ridge, three different kidney systems, the pronephric, mesonephric, and the definitive metanephric kidney, appear in a craniocaudal progression between the third and fourth weeks of gestation. The pronephros is transitory and of little importance except in larval anamniotes. The mesonephros continues the development of the longitudinal collecting duct begun by the pronephros, now referred to as the mesonephric duct. This duct fuses with the cloaca at about 26 days and approximately 2 days later, through an outgrowth, the ureteric bud, induces the metanephros or definitive kidney which establishes functional capacity early in the second half of pregnancy.

It is the mesonephric ducts (the future ductus deferens) which induce the paramesonephric ducts within the intermediate mesodermal ridges. This is the first of those interactions with which we must become familiar. These ducts from which the oviducts and uterus will develop, begin between the fifth and sixth weeks as an invagination of the coelomic epithelium on the anterolateral surface of the intermediate mesodermal ridge parallel to the mesonephric duct. Cranially each duct opens into

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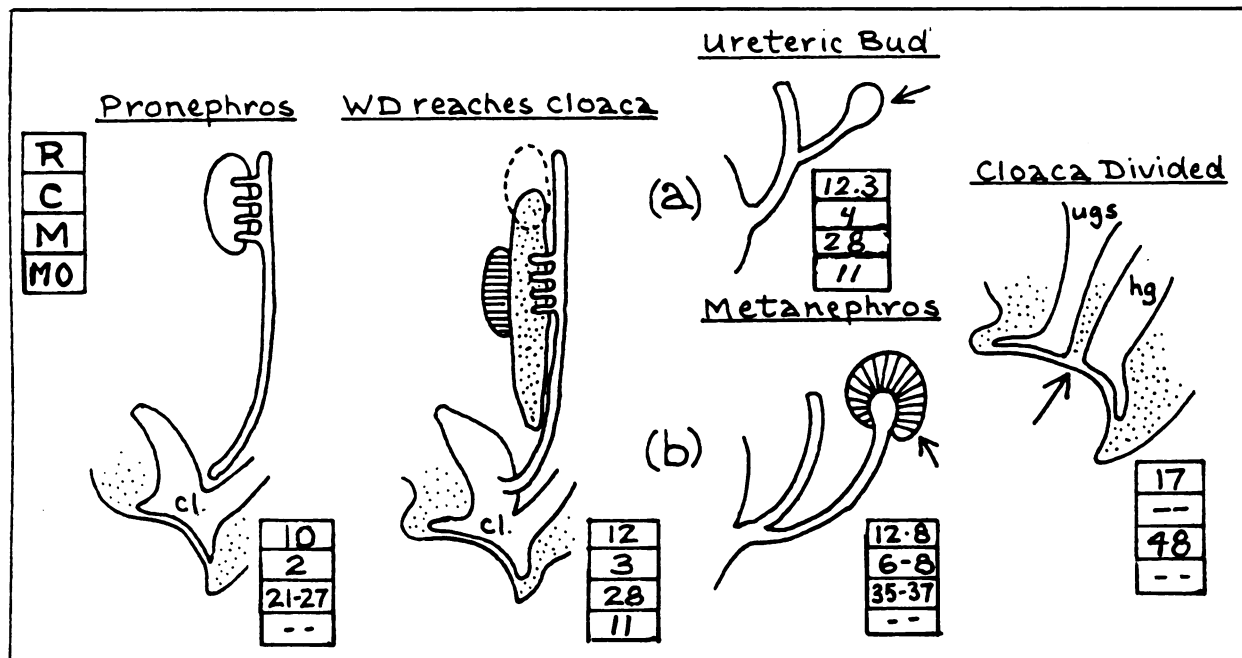


FIGURE 1. Various developmental stages of the urinary system, accompanied by the age in days on which a particular event occurs in the rat (R), mouse (Mo), and man (M) based on fertilization age and in the chick (C) based on incubation age. Modified from Monie (6).

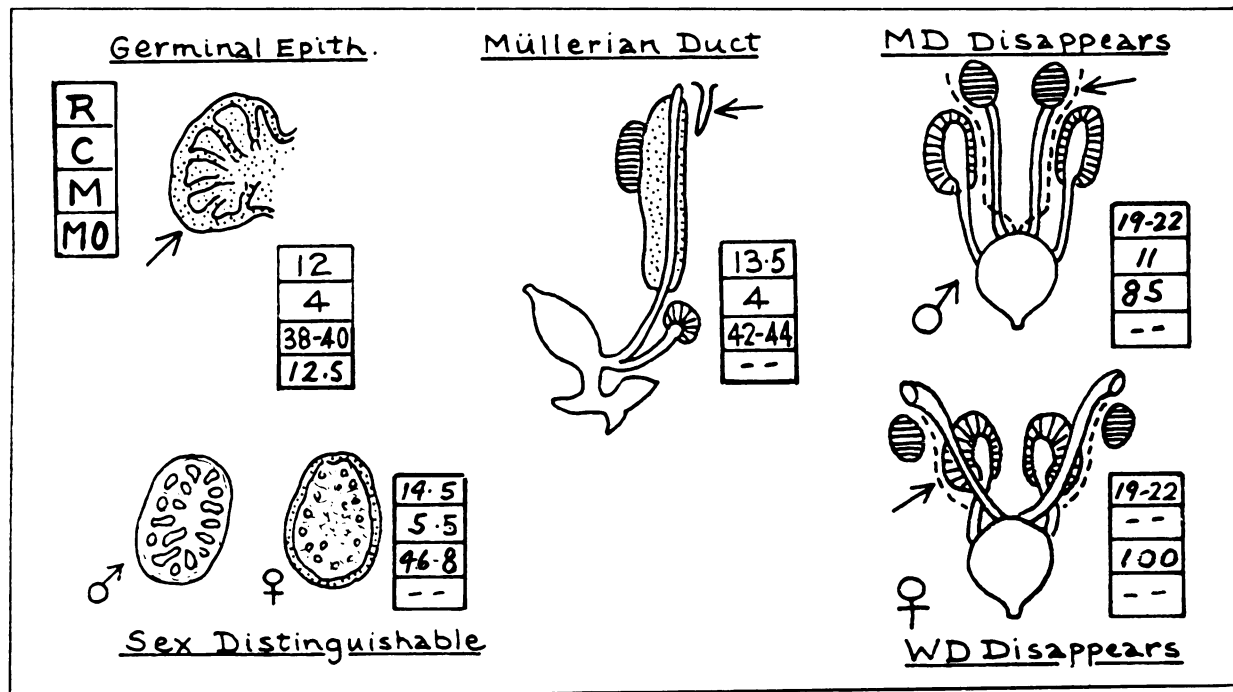


FIGURE 2. Various developmental stages of the reproductive system accompanied by the age in days on which a particular event occurs in the rat (R), mouse (Mo), and man (M) based on fertilization age and in the chick (C) based on incubation age. Modified from Monie (6).

the coelomic cavity (future ostium of the oviduct) and progresses caudally, lateral to the mesonephric duct, crossing it anteriorly and growing caudomedially to meet with the paramesonephric duct from the opposite side at about eight weeks. From this point of juncture, Mueller's tubercle, the ducts fuse for a short distance cranially, and at about nine weeks the wall between them begins to break down, allowing the differentiation of the corpus and cervix of the uterus. As these paramesonephric (Muellerian) ducts join in the midline, having passed antermomedially to assume a position anterior to the developing rectum, they do not break away from the coelomic wall; rather, they stretch those serosal and connective tissue components of the coelomic wall which cover the ducts and fuse these components with those of the opposite side thus forming the embryonic broad ligament in the center of which the developing uterus is located. In the rat, fusion of the paramesonephric ducts does not occur, resulting in two uterine horns; also, the broad ligament does not form, but its components remain simply as the mesenteric support for each of the bilateral uterine horns.

The sex of the human being is determined in the sixth week, for it is then that the primordial germ cells complete their migration from the yolk sac through the posterior gut wall, its dorsal mesentery and into the intermediate mesodermal ridge where, together with the primitive sex cords they establish the indifferent gonad. It is also at this time that the establishment of two pairs of genital ducts, the Wolffian (male) and Muellerian (female) ducts, is completed, and the embryo rests momentarily in an indifferent sexual state. Genetic sex asserts itself, the duct system of the opposite sex disappears almost completely and the remaining system, in this case the paramesonephric ducts, differentiates into final form.

Before we can discuss the development of this final form which includes the induction of the vagina and the differentiation of the cloaca into the external genitalia, we must consider the division of the cloaca into urogenital and anal regions. This is accomplished between the fifth and seventh weeks, during which time a transverse ridge of tissue, the urorectal septum, appears and grows caudally towards the cloacal membrane. When this septum

**Table 1. Comparative urogenital development.**

Event	Man	Rat	Mouse	Chick	Standard Stages	Streeter's Horizons
Allantois appears	16.5		7			
Pronephros appears	22	10			14	X
Mesonephros appears	24	11.5	9.5	3	16	XI
Mesonephric duct enters urogenital sinus	28	12	11		22	XII
Urorectal septum appearing	28-48	12.5-17			18-33	XII-XVIII
Ureteric bud appears	28	12.3	11	4	23	XIII
Ureteric bud with metanephric "cap"	32	12.5			25	XIV
Metanephros	35-37	12.8		6	26	XV
Germinal epithelium	38-40	12	12.5	4	19	XII
Testis histologically differentiated	46-48	13.5		5.5	28	XVII
Paramesonephric duct appears	42-44	13.5		4	28	XVII
Paramesonephric duct reaches cloaca	49-56	15.5			32	XVIII
Degeneration of paramesonephric duct in male	85	19-22		11	35	XXIII
Degeneration of mesonephric duct in female	100	19-22			35	XXIII
Indifferent swellings of external genitalia	37	19			35	XVIII
Urethral groove closed	84	22			35	XVIII

reaches the cloacal membrane, its point of contact is described as the perineal body, and the cloaca itself becomes divided into a urogenital sinus and an anorectal canal covered by a urogenital membrane and an anal membrane. The primitive urogenital sinus is now modified further into a bladder and two structures, the pelvic portion of the urogenital sinus and the definitive urogenital sinus whose ultimate determination and structure also await the expression of the sex of the embryo.

Let us now turn to the development of the vagina, which begins about the ninth week of gestation. Its formation is the second example of induction which was mentioned as a basic concept in the development of the female genital system. The fused tips of the paramesonephric ducts, the Muellerian tubercle, contacts the wall of the urogenital sinus and induces the formation of the vagina. By the fifth month the vaginal outgrowth is canalized but remains separated from the urogenital sinus by the hymen.

All that remains to complete the female genital system is the differentiation of the external genitalia from the primitive urogenital sinus. Before the cloaca was divided by the urorectal septum which occurred during the fifth to seventh week, it was surrounded by elevated cloacal folds which ended in a genital tubercle anteriorly. Following subdivision of the cloaca into a urogenital sinus and an anorectal canal, the cloacal folds surrounding the urogenital sinus becomes the urogenital folds, and these in turn are surrounded by genital swellings (sixth week) which become the labia minora and labia majora respectively. The genital tubercle elongates, becoming the phallus which is modified further into the clitoris.

Let us now turn our attention to the table of development and the sketches which are intended to illustrate it. They are based on the age in days on which a particular event occurs in the organogenesis of man, rat and mouse based on fertilization age and in the chick according to its incuba-

tion age. These figures (Figs. 1 and 2) are not intended to be the "final word", but are approximations included to create a clearer picture of comparative organogenesis.

Because vertebrates exhibit such widely variant periods of development, it is considered easier to compare them on the basis of developmental stages such as Streeter's Horizons (9) or the 36 Standard Stages of Witschi (8). Both of these staging procedures have been included in the developmental table (Table 1) and are broadly organized as follows (Standard in Arabic numerals and Horizons in Roman numerals): cleavage and blastula, 1 to 7 or I to III; gastrula, 8 to 11 or IV to VII; primitive streak, 12 or VIII; neurula, 13 to 17 or IX to XII; tailbud embryo, 18 to 24 or XII to XIII; complete embryo, 25 or XIV; metamorphosing embryo, 26 to 33 or XV to XXII; fetus, 35 to 36 or XXIII.

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